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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet 1 of 13

Complete if Known	
Application Number	10/700,971
Filing Date	November 4, 2003
First Named Inventor	Muthiah Manoharan
Art Unit	1623
Examiner Name	To Be Determined
Attorney Docket Number	CHEM0005US.P1 (ISIC0009-101)

U.S. PATENT DOCUMENTS

Examiner Initials *	Cite No.[1]	Document Number: Number - Kind Code[2] (*if known*)	Publication/Issue Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
	AA	US-5,898,031	04-27-1999	Crooke	
	AB	US-6,107,094	08-22-2000	Crooke	
	AC	US-6,395,492	05-28-2002	Manoharan	
	AD	US-4,958,013	09-18-1990	Letsinger	
	AE	US-6,528,631	03-04-2003	Manoharan	
	AF	US-4,904,582	02-27-1990	Tullis	
	AG	US-5,672,662	09-30-1997	Harris	
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	AM	US-5,272,250	12-21-1993	Spielvogel	
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	AO	US-5,525,465	06-11-1996	Haralambidis	
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	AQ	US-5,545,730	08-13-1996	Urdea	
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Examiner Initials*	Cite No.[1]	Foreign Patent Document: Country Code[3] - Number[4] - Kind Code[5] (*if known*)	Publication Date/Filing Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T[6]
	AU	✓ WO 01/48183	07-05-2001	Devgen NV		
	AV	✓ WO 00/44895	08-03-2000	Kreutzer		
	AW	✓ WO 00/49035	08-24-2000	General Hospital		
	AX	✓ WO 00/63364	10-26-2000	American Home Products Corp.		
	AY	✓ WO 01/36641	05-25-2001	Chiron Corp.		
	AZ	✓ WO 01/36646	05-25-2001	Cancer Research		
	BA	✓ WO 99/32619	07-01-1999	Carnegie Inst. Of Washington		
	BB	✓ WO 00/44914	08-03-2000	Med. College of Georgia		
	BC	✓ WO 01/29058	04-26-2001	Univ. of Mass.		

Examiner Signature		Date Considered	

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Sheet 2 of 13

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	BD	US-5,608,046	03-04-1997	Cook	
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	BF	US-4,667,025	05-19-1987	Miyoshi	
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	BJ	US-5,391,723	02-21-1995	Priest	
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	BX	✓ WO 01/75164	10-11-2001	Whitehead Inst.		
	BY	✓ WO 93/07883	04-29-1993	Isis Pharm.		
	BZ	✓ WO 00/76554	12-21-2000	Isis Pharm.		
	CA	✓ WO 96/11205	04-18-1996	Isis Pharm.		
	CB	WO 98/52614	11-26-1998	Brd. Of Trustees of the Leland Stanford Junior Univ.		

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Art Unit	1623
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Attorney Docket Number	CHEM0005US.P1 (ISIC0009-101)

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	CD	US-5,138,045	08-11-1992	Cook	
	CE	US-5,414,077	05-09-1995	Lin	
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	CU	US-5,371,241	12-06-1994	Brush	
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Sheet 4 of 13

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Application Number	10/700,971
Filing Date	November 4, 2003
First Named Inventor	Muthiah Manoharan
Art Unit	1623
Examiner Name	To Be Determined
Attorney Docket Number	CHEM0005US.P1 (ISIC0009-101)

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	CW	US-5,451,463	09-19-1995	Nelson	
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	CY	US-5,565,552	10-15-1996	Magda	
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	DA	US-5,585,481	12-17-1996	Arnold	
	DB	US-5,587,371	12-24-1996	Sessler	
	DC	US-5,595,726	01-21-1997	Magda	
	DD	US-5,597,696	01-28-1997	Linn	
	DE	US-5,599,923	02-04-1997	Sessler	
	DF	US-5,599,928	02-04-1997	Hemmi	
	DG	US-5,688,941	11-18-1997	Cook	
	DH	US-6,153,737	11-28-2000	Manoharan	
	DI	US-6,172,208	01-09-2001	Cook	
	DJ	US-6,300,319	10-09-2001	Manoharan	
	DK	US-6,335,434	01-01-2002	Guzaev	
	DL	US-6,395,437	05-28-2002	Wollesen	
	DM	US-6,444,806	09-03-2002	Veerapaneni	
	DN	US-6,486,308	11-26-2002	Kutyavin	

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Sheet 5 of 13

Complete if Known	
Application Number	10/700,971
Filing Date	November 4, 2003
First Named Inventor	Muthiah Manoharan
Art Unit	1623
Examiner Name	To Be Determined
Attorney Docket Number	CHEM0005US.P1 (ISIC0009-101)

NON PATENT LITERATURE DOCUMENTS

Examiner Initials *	Cite No.[1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T [2]
	DO	AFONINA, I. et al., "Sequence-specific arrest of primer extension on single-stranded DNA by an oligonucleotide-minor groove binder conjugate," *Proc. Natl. Acad. Sci. USA* (1996) 93:3199-3204.	
	DP	ANTOPOLSKY, M. et al., "Peptide-Oligonucleotide Phosphorothioate Conjugates with Membrane Translocation and Nuclear Localization Properties," *Bioconjugate Chem.* (1999) 10(4):598-606.	
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	DS	ASTRIAB-FISHER, A. et al., "Antisense Inhibition of P-glycoprotein Expression Using Peptide-Oligonucleotide Conjugates," *Biochem. Pharmacol.* (2000) 60:83-90.	
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Sheet 6 of 13

Complete if Known	
Application Number	10/700,971
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First Named Inventor	Muthiah Manoharan
Art Unit	1623
Examiner Name	To Be Determined
Attorney Docket Number	CHEM0005US.P1 (ISIC0009-101)

NON PATENT LITERATURE DOCUMENTS

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	DZ	BRANDEN, L. J. et al., "A peptide nucleic acid-nuclear localization signal fusion that mediates nuclear transport of DNA," *Nature Biotech* (1999) 17:784-787.	
	EA	BRANTL, S., "Antisense-RNA regulation and RNA interference," *Biochimica et Biophysica Acta* (2001) 1575:15-25.	
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	EG	COHEN, G. L. et al., "Sequence Dependent Binding of *cis*-Dichlorodiammineplatinum(II) to DNA," *J. Am. Chem. Soc.* (1980) 102(7):2487-2488.	
	EH	COREY, D. R., "48000-fold Acceleration of Hybridization by Chemically Modified Oligonucleotides," *J. Am. Chem. Soc.* (1995) 117(36):9373-9374.	
	EI	COREY, D. R. et al., "Generation of a Hybrid Sequence-Specific Single-Stranded Deoxyribonuclease," *Science* (1987) 238:1401-1403.	
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	EK	DUFF, R. J. et al., "[17] Intrabody Tissue-Specific Delivery of Antisense Conjugates in Animals: Ligand-Linker-Antisense Oligomer Conjugates," *Methods Eanzymol.* (2000) 313:297-321.	
	EL	EFIMOV, V. A. et al., "Synthesis of Polyethylene Glycol – Oligonucleotide Conjugates," *Bioorg. Khim.* (1993) 19(8):800-804.	
	EM	ELBASHIR, S. M. et al., "RNA interference is mediated by 21- and 22-nucleotide RNAs," *Genes Dev.* (2001) 15:188-200.	
	EN	ELBASHIR, S. M. et al., "Duplexes of 21-nucleotide RNAs mediate RNA interference in cultured mammalian cells," *Nature* (2001) 411:494-498.	
	EO	ELBASHIR, S. M. et al., "Functional anatomy of siRNAs for mediating efficient RNAi in *Drosophila melanogaster* embryo lysate," *EMBO J.* (2001) 20(23):6877-6888.	
	EP	FIRE, A. et al., "Potent and specific genetic interference by double-stranded RNA in *Caenorhabditis elegans*," *Nature* (1998) 391:806-811.	
	EQ	FIRESTONE, R. A., "Low-Density Lipoprotein as a Vehicle for Targeting Antitumor Compounds to Cancer Cells," *Bioconjugate Chem.* (1994) 5:105-113.	
	ER	GORLACH, M. et al., "The mRNA Poly(A)-Binding Protein: Localization, Abundance, and RNA-Binding Specificity," *Exp. Cells Res.* (1994) 211:400-407.	
	ES	GUO, S. et al., "*par-1*, a Gene Required for Establishing Polarity in C. elegans Embryos, Encodes a Putative Ser/Thr Kinase That Is Asymmetrically Distributed," *Cell* (1995) 81:611-620.	
	ET	GURA, T., "A silence that speaks volumes," *Nature* (2000) 404:804-808.	
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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet 8 of 13

Complete if Known	
Application Number	10/700,971
Filing Date	November 4, 2003
First Named Inventor	Muthiah Manoharan
Art Unit	1623
Examiner Name	To Be Determined
Attorney Docket Number	CHEM0005US.P1 (ISIC0009-101)

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials *	Cite No.[1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T [2]
	EV	HALL, J. et al., "Efficient sequence-specific cleavage of RNA using novel europium complexes conjugated to oligonucleotides," *Chem. Biol.* (1994) 1(3):185-190.	
	EW	HARITON-GAZAL, E. et al., "Targeting of Nonkaryophilic Cell-Permeable Peptides into the Nuclei of Intact Cells by Covalently Attached Nuclear Localization Signals," *Biochemistry* (2002) 41(29):9208-9214.	
	EX	HENDERSON, B. R. et al., "A Comparison of the Activity, Sequence Specificity, and CRM1-Dependence of Different Nuclear Export Signals," *Exp. Cell Res.* (2000) 256:213-224.	
	EY	HUANG, L. et al., "Oligonucleotide conjugates of Eu(III) tetraazamacrocycles with pendent alcohol and amide groups promote sequence-specific RNA cleavage," *J. Biol. Inorg. Chem.* (2000) 5:85-92.	
	EZ	HUH, N. et al., "Design, Synthesis, and Evaluation of Mitomycin-Tethered Phosphorothioate Oligodeoxynucleotides," *Bioconjugate Chem.* (1996) 7:659-669.	
	FA	JASCHKE, A. et al., "Synthesis and properties of oligodeoxyribonucleotide-polyethylene glycol conjugates," *Nucleic Acids Res.* (1994) 22(22):4810-4817.	
	FB	JORGENSEN, R. A. et al., "Chalcone synthase cosuppression phenotypes in petunia flowers: comparison of sense vs. antisense constructs and single-copy vs. complex T-DNA sequences," *Plant Mol. Biol.* (1996) 31:957-973.	
	FC	JUBY, C. D. et al., "Facile Preparation of 3'Oligonucleotide-Peptide Conjugates," *Tetrahedron Letters* (1991) 32(7):879-882.	
	FD	KABANOV, A. V. et al., "A new class of antivirals: antisense oligonucleotides combined with a hydrophobic substituent effectively inhibit influenza virus reproduction and synthesis of virus-specific proteins in MDCK cells," *FEBS Lett.* (1990) 259(2):327-330.	
	FE	KRIEG, A. M. et al., "Uptake of Oligodeoxyribonucleotides by Lymphoid Cells Is Heterogeneous and Inducible," *Antisense Research and Development* (1991) 1:161-171.	
	FF	KUIJPERS, W. H. A. et al., "Specific Recognition of Antibody-Oligonucleotide Conjugates by Radiolabeled Antisense Nucleotides: A Novel Approach for Two-Step Radioimmunotherapy of Cancer," *Bioconjugate Chem.* (1993) 4(1):94-102.	

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Sheet 9 of 13

Complete if Known	
Application Number	10/700,971
Filing Date	November 4, 2003
First Named Inventor	Muthiah Manoharan
Art Unit	1623
Examiner Name	To Be Determined
Attorney Docket Number	CHEM0005US.P1 (ISIC0009-101)

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	FG	LETSINGER, R. L. et al., "Cholesteryl-conjugated oligonucleotides: Synthesis, properties, and activity as inhibitors of replication of human immunodeficiency virus in cell culture," *Proc. Natl. Acad. Sci. USA* (1989) 86:6553-6556.	
	FH	LI, S. et al., "Folate-Mediated Targeting of Antisense Oligodeoxynucleotides to Ovarian Cancer Cells," *Pharm. Res.* (1998) 15(10):1540-1545.	
	FI	LIMA, W. F. et al., "Highly efficient endonucleolytic cleavage of RNA by a Cys_2His_2 zinc-finger peptide," *Proc. Natl. Acad. Sci. USA* (1999) 96:10010-10015.	
	FJ	LIN, M. et al., "Inhibition of collagenase type I expression by psoralen antisense oligonucleotides id dermal fibroblasts," *Faseb J.* (1995) 9:1371-1377.	
	FK	LIN, K.-Y. et al., "A Cytosine Analogue Capable of Clamp-Like Binding to a Guanine in Helical Nucleic Acids," *J. Am. Chem. Soc.* (1998) 120(33):8531-8532.	
	FL	LIPARDI, C. et al., "RNAi as Random Degradative PCR: siRNA Primers Convert mRNA into dsRNAs that Are Degraded to Generate New siRNAs," *Cell* (2001) 107:297-307.	
	FM	LIU, K. et al., "Efficient Nuclear Delivery of Antisense Oligodeoxynucleotides and Selective Inhibition of CETP Expression by Apo E Peptide in a Human CETP-Stably Transfected CHO Cell Line," *Arterioscler. Thromb. Vasc. Biol.* (1999) 19:2207-2213.	
	FN	LIXIN, R. et al., "Novel Properties of the Nucleolar Targeting Signal of Human Angiogenin," *Biochem. Biophys. Res. Comm.* (2001) 284:185-193.	
	FO	LUKHTANOV, E. A. et al., "Direct, Solid Phase Assembly of Dihydropyrroloindole Peptides with Conjugated Oligonucleotides," *Bioconjugate Chem.* (1996) 7(5):564-567.	
	FP	MANOHARAN, M., "Oligonucleotide Conjugates in Antisense Technology," *Antisense Drug Technology, Principles, Strategies, and Applications*, Crooke, S. T. ed., Marcel Dekker, New York, (2001) Chapter 16, 391-467.	
	FQ	MANOHARAN, M. et al., "Novel Functionalization of the Sugar Moiety of Nucleic Acids for Multiple Labeling in the Minor Groove," *Tetrahedron Letters* (1991) 32(49):7171-7174.	

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Sheet 10 of 13

Complete if Known	
Application Number	10/700,971
Filing Date	November 4, 2003
First Named Inventor	Muthiah Manoharan
Art Unit	1623
Examiner Name	To Be Determined
Attorney Docket Number	CHEM0005US.P1 (ISIC0009-101)

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	FR	MANOHARAN, M., "Oligonucleotide Conjugates as Potential Antisense Drugs with Improved Uptake, Biodistribution, Targeted Delivery and Mechanism of Action," *Antisense & Nucleic Acid Drug Development* (2002) 12:103-128.	
	FS	MANOHARAN, M., "Designer Antisense Oligonucleotides: Conjugation Chemistry and Functionality Placement," *Antisense Research and Applications*, Crooke and Lebleu, eds., CRC Press Boca Raton, FL (1993) Chapter 17, 303-349.	
	FT	MANOHARAN, M. et al., "Lipidic Nucleic Acids," *Tetrahedron Lett.* (1995) 36(21):3651-3654.	
	FU	MARTINEZ, J. et al., "Single-Stranded Antisense siRNAs Guide Target RNA Cleavage in RNAi," *Cell* (2002) 110:563-574.	
	FV	MARUENDA, H. et al., "Antisense Sequence-Directed Cross-Linking of DNA Oligonucleotides by Mitomycin C," *Bioconjugate Chem.* (1996) 7(5):541-544.	
	FW	MARUENDA, H. et al., "Antisense sequence-directed cross-linking of RNA oligonucleotides by mitomycin," *Anti-Cancer Drug. Des.* (1997) 12:473-479.	
	FX	MELLITZER, G. et al., "Spatial and temporal 'knock down' of gene expression by electroporation of double-stranded RNA and morpholinos into early postimplantation mouse embryos," *Mechanisms of Development* (2002) 118:57-63.	
	FY	MEUNIER, L. et al., "The nuclear export signal-dependent localization of oligonucleopeptides enhances the inhibition of the protein expression from a gene transcribed in cytosol," *Nucleic Acids Res.* (1999) 27(13):2730-2736.	
	FZ	MILI, S. et al., "Distinct RNP Complexes of Shuttling hnRNP Proteins with Pre-mRNA and mRNA: Candidate Intermediates in Formation and Export of mRNA," *Mol. Cell Biol.* (2001) 21(21):7307-7319.	
	GA	MISHRA, R. K. et al., "Improved leishmanicidal effect of phosphorotioate antisense oligonucleotides by LDL-mediated delivery," *Biochim. Biophys Acta.* (1995) 1264:229-237.	
	GB	MONTGOMERY, M. K. et al., "RNA as a target of double-stranded RNA-mediated genetic interference in *Caenorhabditis elegans*," *Proc. Natl. Acad. Sci. USA* (1998) 95:15502-15507.	

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Filing Date	November 4, 2003
First Named Inventor	Muthiah Manoharan
Art Unit	1623
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	GC	NAPOLI, C. et al., "Introduction of a Chimeric Chalcone Synthase Gene into Petunia Results in Reversible Co-Suppression of Homologous Genes *in trans*," *Plant Cell* (1990) 2:279-289.	
	GD	NELSON, P. S. et al., "Bifunctional oligonucleotide probes synthesized using a novel CPG support are able to detect single base pair mutations," *Nucleic Acids Res.* (1989) 17(18):7187-7194.	
	GE	NISHIKURA, K. et al., "A Short Primer on RNAi: RNA-Directed RNA Polymerase Acts as a Key Catalyst," *Cell* (2001) 107:415-418.	
	GF	OBERHAUSER, B. et al., "Effective incorporation of 2'-O-methyl-oligoribonucleotides into liposomes and enhanced cell association through modification with thiocholesterol," *Nucleic Acids. Res.* (1992) 20(3):533-538.	
	GG	PARRISH, S. et al., "Functional Anatomy of a dsRNA Trigger: Differential Requirement for the Two Trigger Strands in RNA Interference," *Molecular Cell* (2000) 6:1077-1087.	
	GH	PICHON, C. et al., "Intracellular Routing and Inhibitory Activity of Oligonucleopeptides Containing a KDEL Motif," *Mol. Pharmacol.* (1997) 51:431-438.	
	GI	PRAKASH, T. P. et al., "Synthesis of Site-Specific Oligonucleotide-Polyamine Conjugates," *Bioorg. Med. Chem. Lett.* (1994) 4(14):1733-1738.	
	GJ	RAJUR, S. B. et al., "Covalent Protein-Oligonucleotide Conjugates for Efficient Delivery of Antisense Molecules," *Bioconjugate Chem.* (1997) 8(6):935-940.	
	GK	RHODES, J. et al., "Therapeutic potentiation of the immune system by costimulatory Schiff-base-forming drugs," *Nature* (1995) 377(6544):71-75.	
	GL	RUMP, E. T. et al., "Preparation of Conjugates of Oligodeoxynucleotides and Lipid Structures and Their Interaction with Low-Density Lipoprotein," *Bioconjugate Chem.* (1998) 9(3):341-349.	
	GM	SAISON-BEHMOARAS, T. et al., "Short modified antisense oligonucleotides directed against Ha-*ras* point mutation induce selective cleavage of the mRNA and inhibit T24 cells proliferation," *EMBO J.* (1991) 10(5):1111-1118.	

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Filing Date	November 4, 2003
First Named Inventor	Muthiah Manoharan
Art Unit	1623
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	GN	SCHWARZ, D. S. et al., "Evidence that siRNAs Function as Guides, Not Primers, in the *Drosophila* and Human RNAi Pathways," *Molecular Cell* (2002) 10:537-548.	
	GO	SHEA, R. G. et al., "Synthesis, hybridization properties and antiviral activity of lipid-oligodeoxynucleotide conjugates," *Nucleic Acids Res.* (1990) 18(13):3777-3783.	
	GP	SIJEN, T. et al., "On the Role of RNA Amplification in dsRNA-Triggered Gene Silencing," *Cell* (2001) 107:465-476.	
	GQ	SVINARCHUK, F. P. et al., "Inhibition of HIV proliferation in MT-4 cells by antisense oligonucleotide conjugated to lipophilic groups," *Biochimie* (1993) 75:49-54.	
	GR	TABARA, H. et al., "RNAi in *C. elegans*: Soaking in the Genome Sequence," *Science* (1998) 282:430-431.	
	GS	TAMANINI, F. et al., "The fragile X-related proteins FXR1P and FXR2P contain a functional nucleolar-targeting signal equivalent to the HIV-1 regulatory proteins," *Hum. Mol. Genet.* (2000) 9(10):1487-1493	
	GT	TIJSTERMAN, M. et al., "RNA Helicase MUT-14-Dependent Gene Silencing Triggered in *C. elegans* by Short Antisense RNAs," *Science* (2002) 295:694-697.	
	GU	TIMMONS, L. et al., "Specific interference by ingested dsRNA," *Nature* (1998) 395:854.	
	GV	TIMMONS, L. et al., "Ingestion of bacterially expressed dsRNAs can produce specific and potent genetic interference in *Caenorhabditis elegans*," *Gene* (2001) 263:103-112.	
	GW	TUSCHL, T. et al., "Targeted mRNA degradation by double-stranded RNA in vitro," *Genes Dev.* (1999) 13:3191-3197.	
	GX	WADA, A. et al., "Nuclear export of actin: a novel mechanism regulating the subcellular localization of a major cytoskeletal protein," *EMBO J.* (1998) 17:1635-1641.	

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	GY	WANG, X. et al., "Modular Recognition of RNA by a Human Pumilio-Homology Domain," *Cell* (2002) 110:501-512.	
	GZ	WEI, Z. et al., "Hybridization properties of oligodeoxynucleotide pairs bridged by polyarginine peptides," *Nucleic Acids Res.* (1996) 24(4):655-661.	
	HA	WEIN, G. et al., "The 3'-UTR of the mRNA coding for the major protein kinase C substrate MARCKS contains a novel CU-rich element interacting with the mRNA stabilizing factors HuD and HuR," *Eur. J. Biochem.* (2003) 270:350-365.	
	HB	YANG, Y. et al., "HIV-1 TAT-mediated protein transduction and subcellular localization using novel expression vectors," *FEBS Letters* (2002) 532:36-44.	
	HC	ZANTA, M. A. et al., "Gene delivery: A single nuclear localization signal peptide is sufficient to carry DNA to the cell nucleus," *Proc. Natl. Acad. Sci. USA* (1999) 96:91-96.	
	HD	ZHANG, Z. et al., "Uptake of *N*-(4'-pyridoxyl)amines and release of amines by renal cells: A model for transporter-enhanced delivery of bioactive compounds," *Proc. Natl. Acad. Sci. USA* (1991) 88:10407-10410.	
	HE	ZHU, T. et al., "Oligonucleotide-Poly-L-ornithine Conjugates: Binding to Complementary DNA and RNA," *Antisense Res. Dev.* (1993) 3:265-275.	
	HF	ZUCKERMANN, R. N. et al., "Site-Selective Cleavage of RNA by a Hybrid Enzyme," *J. Am. Chem. Soc.* (1988) 110:1614-1615.	

Examiner Signature	/Sean Mcgarry/	Date Considered	05/27/2008

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